An Improved Intravenous Contrast Medium

Preliminary Studies with Hypaque®

JACK E. ENGELHARDT, M.D., Corona Del Mar, and
GEORGE JACOBSON, M.D., Los Angeles

• **A relatively new intravenous opaque medium, Hypaque® in 50 per cent solution, was used in 50 consecutive patients. None of them had a serious reaction. Twenty-two had mild reactions which were of no clinical significance. The radiographs obtained seemed to be equal in quality to those obtained with other contrast media.**

DURING THE last two decades there have been many substances used for intravenous urography and constant work is being done to develop a contrast medium which is nontoxic and has a good radiographic density. The purpose of this presentation is to report on the use of a new iodine-containing compound, Hypaque,® in 50 consecutive examinations.

Hypaque (sodium 3,5-diacetamido-2,4,6-triiodobenzoate) is a white crystalline solid which contains 59.87 per cent iodine and is highly soluble in water. The iodine content of Hypaque is slightly less than that of Urokon® (sodium acetrizoate 3-acetylamino-2,4,6-triiodobenzoic acid) which contains 65.8 per cent iodine. Diodrast® (3,5-diiodo-4-pyridone-N-acetic acid diethanolamine) contains 49.8 per cent iodine and Neo-iopax® (sodium iodomethamate, disodium salt of N-methyl-3,5-diiodochelidamic acid) contains 51.5 per cent iodine.

In anesthetized dogs, rapid injection of Hypaque in dosage up to 4,000 mg. per kilogram of body weight produced no change in the heart rate, blood pressure, respiration, or autonomic function.[5] At a dosage of 8,000 mg. per kilogram, respiratory arrest and later cardiac arrest occurred. It was also found that there was slight inversion of the terminal portion of the T-wave at the 1,000, 2,000, 4,000 mg. per kilogram dose levels. The compound was excreted almost entirely through the kidneys. The rate of excretion was rapid since most of the administered drug was eliminated within two hours and over 90 per cent was excreted within 24 hours. Porporis[3] has reported similar results in excretion studies using Urokon.

In tests with rats, cats and mice, it was observed that the acute toxicity of Hypaque was less than that of other contrast media.[5] Rhesus monkeys receiving Hypaque intravenously had no casts in the collecting tubules whereas in monkeys receiving various other media, casts developed in the collecting tubules of the kidneys. With toxic doses, Hypaque and the other contrast media produced similar reversible pathological changes in the kidneys, liver and lungs.

All material used in this study was supplied by Winthrop-Stearns, Inc.

From the Departments of Radiology, School of Medicine, University of Southern California, and the Los Angeles County General Hospital.

Submitted July 22, 1955.

METHOD OF STUDY

The patients were prepared for excretory urography in the usual manner. Before injection, a history was obtained with regard to allergic sensitivity and previous reactions to other compounds containing iodine. Temperature, pulse rate, respiration rate and blood pressure were recorded before the radio-

TABLE 1.—*Reactions in 50 Patients Following Intravenous Injection of 30 cc. of 50 Per Cent Hypaque®*

Symptoms	No. Patients with Reaction	Severity	Duration
Nausea	4	Minimal	1 or 2 minutes
Vomiting	0		
Excessive sweating	1	Minimal	Seconds
Excessive salivation	2	Minimal	During entire examination
Choking sensation	0		
Wheezing	0		
Dyspnea	0		
Cyanosis	0		
Flushing of skin	2	Minimal	2 to 3 minutes
Extreme pallor	0		
Pruritus	0		
Facial edema	0		
Sneezing	0		
Urticaria	1	Localized to neck, minimal	3 minutes
Venospasm (Local infiltration?)	2	Mild	3 minutes to few seconds
Other reactions—Bitter taste, peculiar taste	4	Mild	Few minutes
Elevation of temperature 1½ minutes after injection	1	Minimal	
Fall in systolic blood pressure	4	Minimal	
Increase in pulse	1	Minimal	
Total	22		

graphic examination was begun. A sensitivity test, in which 2 cc. of Hypaque was injected intravenously, was done in each case. Following this, 30 cc. of 50 per cent Hypaque was injected in approximately 30 to 45 seconds. Fifteen and thirty minutes after injection, the pulse, temperature, respiration and blood pressure were again recorded. All reactions, even those of a minor nature, were tabulated (Table 1). Radiographs were taken at 5, 10, 25, and 45 minutes after injection of Hypaque.

REACTIONS

In 50 consecutive examinations, there were 22 patients who had minor reactions (Table 1). Immediately after injection, four patients experienced a slightly bitter or metallic taste. During the first 15 minutes after injection, four patients had a decrease in systolic blood pressure ranging from 10 to 20 mm. of mercury. However, the blood pressure was back to normal at the termination of the examination. Two patients had slight pain in the shoulder which could have been attributed to venospasm. The pain lasted a few seconds in one patient, and in the other it persisted for two or three minutes. One patient had mild urticaria. It was localized to the neck.

The remaining ten patients had minimal symptoms which included slight nausea or a slight feeling of flushing. None of the patients had severe nausea and none vomited. All of the reactions recorded were minor and were considered insignificant.

The series was too small, of course, to permit acceptable conclusions, but the incidence of reactions compared very favorably with the incidence reported with Diodrast,[2] Neo-iopax[4] and Urokon.[1]

Although no specific measurements were made of the density of the excreted contrast medium, it was the impression of the authors that the radiographs were equal in quality to those obtained with other contrast media.

205 Carnation Avenue, Apartment 312, Corona Del Mar.

REFERENCES

1. Friedman, L. J., Friedenberg, R., and Love, L.: Intravenous urography by rapid injection; further results with an improved method, A. J. R., 67:433-441, March 1953.

2. Pendergrass, E. P., Chamberlin, G. W., Godfrey, E. W., and Burdick, E. D.: A survey of deaths and unfavorable sequelae following the administration of contrast media, A. J. R., 48:741-762, Dec. 1942.

3. Porporis, A. A., Gladden, V. E., Fischer, G. L., and Mueller, C. B.: The mechanism of Urokon excretion, A.J.R., 72:995-1003, Dec. 1954.

4. Robbins, L. L., Colby, F. H., Sosman, J. L., Eyler, W. R.: Excretory urography: A clinical trial of a new contrast medium (sodium 3-acetylamino-2,4,6-triiodobenzoate), Radiology, 56:684-688, May 1951.

5. Winthrop-Stearns, Inc.: Laboratory data from Department of Medical Research.